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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/003,907	11/02/2001	Subramaniam Srikumaran	UNL 3060.2	7717

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EXAMINER
LI, BAO Q

ART UNIT	PAPER NUMBER
1648	7

DATE MAILED: 04/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/003,907	SRIKUMARAN, SUBRAMANIAM	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *22-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-21 in the scope of BoLA-Ao A11 as the allele specific peptide, bovine respiratory syncytial virus as the viral peptide and HSP 90 as the family of the heat shock proteins as the complex in Paper No. 6 is acknowledged. The traversal is on the ground(s) that the further election of the allele specific peptide, the viral peptide and HSP should be a species election since the claims generically define the invention as a method for eliciting an immune response against a bovine virus comprising administering a combination of at least one bovine viral peptide and at least one heat shock protein as a complex.

2. Applicant's argument has been respectfully considered and the election of the allele specific peptide, viral peptide and heat shock protein is converted to the species elections. Therefore, claims 1-21 in the scope of BoLA-Ao as the allele specific peptide, bovine respiratory syncytial virus as the viral peptide and HSP 90 as the family of the heat shock proteins are considered before examiner.

3. Applicants are reminded to cancel the claims 22-39 drawn to the non-elected groups.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 1 is vague and indefinite in that the metes and bounds of the intended viral epitops are not defined. Each of the intended epitops should be identified with a precise sequence structure. In addition, the intended heat shock protein is not intended. The claim has been interpreted in light of the specification and since the specification fails to set forth the intended boundaries, the claim is indefinite. Consequently, the intended complex is not defined. This affects the dependent claims.

7. Claim 2 is vague and indefinite; the intended "supermotif" is not defined. The claim has been interpreted in light of the specification and since the specification fails to set forth the intended boundaries the claim is indefinite.

8. Claim 3 is vague and indefinite in that the intended " allele specific epitope motif" is not defined. The claim is interpreted in light of the specification; however, since the specification fails to set forth the intended boundaries the claim is indefinite.

9. Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: constructing an epitope/heat shock protein complex and isolating the complex in vivo.

Claim Rejections - 35 USC § 101

10. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. The invention of claims 1, 12 and 14 are directed to non-statutory subject matter. The claimed method read on a nature process of a virus infection because claimed complex used for inducing the immune response is naturally formed in vivo during the natural process of a virus infection, which are considered to be non-statutory and non-patenable subject matter within the scope of 35 U.S.C. 101. See Official Gazett, 1077 O.G. April 21, 1987. Please clarify.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a **written description** of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 2-4 and 21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

14. In the In the instant case, Applicants were not in the possession of a method for eliciting an immune response by using a complex comprising at least one allele specific peptide motif or a supermotif and a heat shock protein to inducing an immune response because the specification does not teach or describe precisely what the structural characteristic of a supermotif or an allele specific peptide motif of BoLA-A11 are.

See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed, Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.

See also *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding

human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

The case law of *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016, which teach that the disclosure of a process for obtaining cDNA and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism. 35 USC 112 requires inter alia that "a patent specification contain a written description of the invention and the manner and process of making and using it in such full clear and concise terms as to enable one skilled in the art to make and use the invention". Case law has made it clear that the requirements for a "written description" and an "enabling disclosure" are separate. For example, where a specification contains sufficient information to enable a skilled chemist to produce a particular compound because it gives detailed information on how to produce analogous compounds but it makes no reference to the compound in question, the "written description" requirement has not been met even though the description may be enabling. In the instant case, the specification has made no reference to the structure of BoLA-A11 or an allele specific peptide motif of BoLA-A11 or supermotif motif in questions.

Claim Rejections - 35 USC § 112

15. Claims 1-21 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for eliciting an immune response by using a immune complex comprising a heat shock protein fused or conjugated with a viral antigen protein or viral antigen peptide in vitro or expressed by a cell line, does not reasonably provide enablement for using an immune complex to induce an immune response, wherein the complex comprising at least one heterologous or homologous heat shock protein and a viral epitope generated in vitro and in vivo. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

16. The test of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art would undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and gain in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988). These factors include the following:

17. 1) & 2) State of art and Unpredictable of the filed. The art at the time of invention was filed has taught that a homologous heat shock fusion protein comprising an antigen epitope can be isolated from an viral infected animal or a viral epitope/heterologous heat shock protein complex can be made in vitro. However, the state of art has not taught how to generate a heterologous heat shock protein/a viral epitope complex in vivo and then use the heat shock protein to induce an immune response specifically against the viral antigen, but not the heat shock protein. However, it is unpredictabl that the use of a heterologous heat shock protein as a complex will induce an immune response against the heterologous heat shock protein too.

18. 3) Number of working examples. Applicants only present general steps of conjugating proteins or protein polypeptide with HSP or expressing a recombinant protein of HSP. However, the specification presents no working examples of the claimed invention, e.g. how to conjugate an bovine viral antigen epitope with a heat shock protein gp96 and isolate the complex ***in vivo,*** then administer the complex in bovines to induce a specific immune response to the bovine viral antigen of RSV. Specification does not teach what the structure of the claimed bovine RSV antigen epitope sequence and how to select 5-25 amino acids from viral antigen of bovine RSV or a bovine BoLA-A11 because claim 1 read broadly on any or all bovine viral antigen.

19. 5) Scope of the claims. The claimed invention read on a method of isolating an heat shock protein complex formed in vivo comprising a heterologous heat shock protein and a viral antigen epitope or B RSV and using the same complex to induce an bovine viral specific immune response against bovine RSV.

20. 6) & 7) Level of the skill in the art and nature of the invention. In order to avoid to induce a non-specific immune response to the heat shock protein, the invention involves one of the most complicated filed of selecting a suitable heterologous heat shock protein sequence, which would

be a proper chaperoned to the viral antigen peptide but not produce an immune response in the host. This level of technique is high and unpredictable. Applicants have general statements regarding to induce an immune response with a heat shock protein/bovine viral epitope complex. However, with regard to an unpredictable filed, this does not constitute an adequate disclosure. See Fiers v. Revel (25USPQ2d 1601 at 1606; and also decision by the Federal Circuit with regard to the enablement issues see Genentech Inc. v. Novo Nordisk A/S, 42 USPQ2d 1001-1007). For example, the CAFC stated that "It is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of an invention in order to constitute enablement." (See page 1005 of the decision).

21. Given the above analysis of the factors which the courts have determined are critical in asserting whether a claimed invention is enabled, it must be considered that the skilled artisan would have had to conduct undue and excessive experimentation in order to practice the claimed invention.

Double Patenting

22. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

23. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

24. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

25. Claims 1-21 provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim1, 4-22 of copending Application No. 09/705,603. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed inventions in both applications all derived to a method for eliciting an immune response against a bovine virus comprising combining at least one bovine viral epitope and at least one heat shock protein to form a purified epitope/heat shock protein complex, and administering an immune system the immune complex to the animals, in which the scope of claimed inventions are overlapping.

26. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

27. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

28. Claims 1-11, 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gaddum et al. (Veterinary Immunology and Immunopathology 1996, Vol. 54, pp. 211-219) and Blachere et al. (J. Exp. Med. 1997, Vol. 186, pp. 1315-1322).

29. Claimed invention is directed to a method of inducing an immune response against bovine viral antigen, preferably to the bovine respiratory syncytial virus (RSV) comprising administering an immune complex comprising a heat shock protein, preferable HSP 90 family of protein with a bovine viral epitope of preferably the bovine RSV.

30. Gaddum et al. taught several allele–specific motif of bovine RSV binding to bovine MHC class I allele A11 and these motifs are all potential CTL epitopes for inducing cytotoxic T cell immune response, wherein the antigen epitope are all 10 amino acids in length (see table 3 on

page 216). Gaddum et al. differ in that they did not teach the bovine RSV epitope conjugated or fused with a heat shock protein.

31. Blachere et al. teach that heat shock protein (HSP) preparations derived from cancer cells and virus-infected cells have been shown previously to elicit cancer-specific or virus –specific immunity. The immunenogenicity of HSV here demonstrate that immunogenic HSV-peptide complexes can also reconstituted in vitro. They explicitly teach the methods of forming complexes of HSP 70 or HSP 96 with a variety of synthetic peptide can be generated in vitro and they are used for inducing an antigen specific T cell immune response (See entire document). They differs from the claimed invention in that they did not specifically teach the complex is made by bovine RSV allele specific peptide motif and HSP gp96.

32. However, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by the recited references and to combine teachings by Gaddum et al. and Blachere et al. to make a fusion protein with either a heterologous HSP or a homologous HSP fused or bond with a bovine RSV allele specific peptide motif to induce an immune response after administering the complex into the animals such as a ruminant or a Bos without unexpected results. As there are no unexpected results have been provided, hence the claimed invention as a whole is prima facie obvious absence unexpected results.

33. Regarding to the supermotif f claim 2, because specification does not disclose what the structure of the supermotif is, the supermotif can be explained as the allele specific motifs that are able to stimulate the CTL immune response as they are disclosed by Gaddum et al.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 7:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li

March 31, 2003

JAMES HOUSEL 4/7/03
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600